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Spatial intralobar correlation of spike and slow wave activity localisations in focal epilepsies: A MEG analysis

M. Kaltenhäuser,* G. Scheler, S. Rampp, A. Paulini, and H. Stefan

Epilepsycenter (ZEE), Department of Neurology, University of Erlangen-Nürnberg, Schwabachanlage 16, D-91054 Erlangen, Germany

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12 patients with focal epilepsy were examined by magnetoencephalography (MEG). Source localisations of interictal epileptiform activity (spikes) yielded clear results. Slow wave dipole density in the frequency range from 2 to 6 Hz, using time selections from an automatic principal component analysis (PCA), was calculated.

Results of spike and slow wave dipole density localisations were superimposed on MR-images of each patient. Slow wave dipole densities were increased close to spike localisations. Distances between spike center of mass and slow wave maxima were calculated, average mean distance was 2.0 cm.

Independant of the localisation in either TLE or ETLE a concordance of slow wave and spike localisations were found. Slow wave localisations were found in patients with lesions in MRI and patients with no abnormalities on the MRI.

In comparison to healthy subjects, slow wave dipole density in patients with epilepsy was clearly increased.

The localisation of slow wave dipole density yielded additional important information and may contribute to defining the irritative zone.

Keywords: Magnetoencephalography; Slow wave dipole density; Interictal spike; Focal epilepsy; Focus localisation

Introduction

Candidates for epilepsy surgery require precise focus localisation. Conventionally, source localisations depend on the occurrence of interictal epilepiform discharges (IED). But IED during MEG-recordings are only found in up to 70% of epilepsy patients (Stefan et al., 2003). Interictal epileptic activity can be precipitated by sleep deprivation or medication (Kettenmann et al., 2005) when there is an absence of epileptic spikes. Looking for additional alternatives to gain information from MEG data, investigation of slow wave brain activity seems to be a promising option.

Slow wave activity in patients with epilepsy is considered to be pathological. Hughes and Wang showed a correlation between slow and sharp waves in EEG and clinical seizure frequency (Hughes and Wang, 2002).

MEG localisations of slow wave activity have been shown in patients with e.g. schizophrenia (Wienbruch et al., 2003), transient ischemic attacks (Stippich et al., 2000), Alzheimer's disease (Fernandez et al., 2002) and brain tumors (Kamada et al., 2001).

Localisation of slow wave activity in epilepsy patients is a quite new approach. Concerning lateralisation, no disagreement was shown between localisation of trains of rhythmic slow wave and interictal spike activity in patients with mesial temporal lobe epilepsy, investigated by means of MEG (Ishibashi et al., 2002). As well, localisation of slow wave activity in patients with tumor-associated epilepsy was investigated by Baayen et al. (2003). They found increased slow wave activity localised in the border zone of the tumor and sometimes within the tumor. The usefulness of localisation of low-frequency dipole density together with localisation of spike activity in patients with temporal lobe epilepsy has been discussed by Fernandez et al. (2004), who conclude that both slow wave and spike analysis are valuable for presurgery epilepsy diagnostics in TLE patients.

To obtain this additional information in patients with cryptogenic and symptomatic focal epilepsies an algorithm based on investigations of Vieth et al. (1996) was used. This step was followed by a new algorithm, partly automated, to localise slow wave activity in the MEG data.

Methods

12 Patients (5 females, 7 males; mean age 29 years, range 18 to 42 years) with a clear epileptic focus localised by interictal MEG spike analysis and presurgical evaluation (long-term EEG, PET, SPECT) as well as 5 healthy subjects (3 females, 2 males; mean age 32 years, range 19 to 44 years) were included in this study. 7 of the 12 patients underwent epilepsy surgery, and 4 of these 7 with intraoperative electrocorticography (ECoG).

Abbreviations: MEG, Magnetoencephalography; EEG, Electroencephalography.

* Corresponding author. Fax: +49 9131 85 36469.
E-mail address: martin.kaltenhaeuser@neuro.imed.uni-erlangen.de (M. Kaltenhäuser).

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MEG-data of patients and healthy subjects were recorded using a Magnes II System (4D-Neuroimaging, San Diego, CA) consisting of two 37-MEG-channel devices. In patients, the positioning of the MEG-sensors was done after video-EEG-monitoring and MRI and with the previous findings. Informed consent was obtained from all participants. Spontaneous brain activity was recorded simultaneously with 31 EEG-channels covering the whole head in the group of patients, healthy subject were investigated without EEG. Investigations were recorded continuously, acquisition time was between 15 and 30 min for each sensor position, using a sample rate of 520 Hz, a band pass filter from 0.1 Hz to 100 Hz.

In healthy subjects, using left and right temporal hemisphere sensors, 10 datasets were produced and investigated.

Spike analysis

Interictal spike analysis and localisation was done according to the standards of our lab (Stefan et al., 2004). Data were filtered offline digitally with a band pass filter from 1 to 70 Hz and notch filtering of 50 Hz. Visual inspection of time series, selection of spikes, single dipole fit with a homogeneous sphere model as distributed by Magnes-Software (4D-Neuroimaging, San Diego, CA) were performed. Best fitting dipoles were selected using quality criteria correlation between measured and single dipole magnetic field distribution ($c>0.97$) and confidence volume of single dipol ($C<1$ cm^3) (Stefan et al., 2003).

Slow wave data analysis

Only those runs were examined, which had been used for spike analysis and yielded clear results. Continuous time intervals of 10 min duration in each patient were used for slow wave analysis.

Digital filtering with a narrow band pass from 2 to 6 Hz was used. Based on the results of a principal component analysis (PCA) time intervals were selected with a total duration of approximately 10 s, in which the MEG data was described by just one component. All time intervals found by PCA were used for calculating single dipole fit localisations using homogeneous sphere model and resulting in high number of single dipoles, typically 5000. As quality selection criterion, a correlation threshold ($c>=0.80$) was used to eliminate all fits with unacceptable deviation between calculated and measured data (Kamada et al., 2001).

Slow wave dipole density was calculated for each voxel of 1 ml by counting the dipoles within the voxel, divided by the number of all dipoles. This provided a percentage-value to each millilitre-voxel

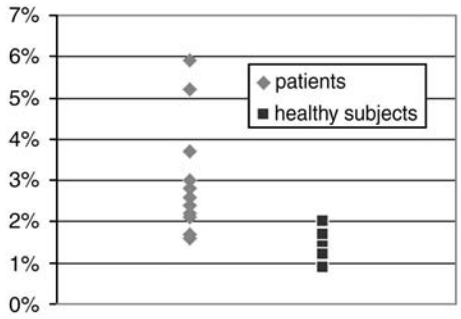

Fig. 1. Slow wave dipole density, maximum percentage within one voxel (pswd_max): comparison of patients and healthy subjects.

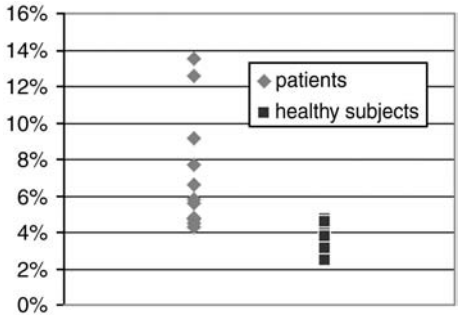

Fig. 2. Slow wave dipole density, sum of percentage in three voxels with most slow wave dipoles (pswd_3v): comparison of patients and healthy subjects.

(percentage of slow wave dipoles within one voxel, "pswd") and therefore characterised the relative slow wave dipole density for this voxel.

MRI was performed in all patients (MPRAGE, 144 slices sagittal, 256 * 256 voxel). Using three fiducial markers, a coordinate system was defined which allowed the results of spike localisations and slow wave dipole density to be overlaid the anatomical MR-slices of the patients.

Comparison of spike localisations and slow wave dipole density

Visual inspection of MEG data was necessary to identify interictal spikes for spike analysis, but not to search for slow wave activity, since the automatic algorithm using a principal component analysis (PCA) is selecting time intervals for slow wave dipole fit, typically the sum of these intervals is 10 s out of 600 s of the investigated time series.

It can not be excluded that rarely interictal spikes or artifacts from eye movement or ECG are just within a PCA-selected time interval.

The results of slow wave dipole density are stable if time intervals containing these artifacts are manually deselected from dipole density calculation. This was checked for all data sets. Therefore, the slow wave dipole density results presented here are not influenced by interical spike nor by artifacts.

Three parameters were established to separate typical random slow wave dipole density distributions which were found in healthy subjects, from those in patients:

"pswd_max": Maximum of pswd
"pswd_3v": Sum of pswd over three voxels with the highest pswd
"pswd_>1%": Sum of pswd over all voxels with pswd more than 1%.

In patients, center of mass of the spike localisations was computed and the distance to voxels with slow wave dipole density maximum was calculated.

Results

Comparison of slow wave dipole densities in patients and healthy subjects

Patients showed maxima from 1.6% to 5.9%, whereas healthy subjects exhibited a maximal pswd (pswd_max) in the range from